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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,838	04/27/2001	Aftab Alam	P108904-00002	8708

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,838	ALAM, AFTAB	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO AMENDMENT, REMARKS, TERMINAL DISCLAIMER, STATUS OF THE APPLICATION AND CLAIMS

1. The amendment, remarks and terminal disclaimer (T.D.) filed 1/12/2004 are acknowledged, entered and considered. In view of Applicant's request claims 1, 2, 14, 16, 18 and 23 have been amended. Thus, claims 1-23 are now pending in the application. The rejection under obviousness-type double patenting over the claims of U.S. Patent No. 5,900,376 and partial rejection under 35 U.S.C. 112, second paragraph are withdrawn in view of Applicant's amendment, remarks and submission of T.D. filed 1/12/04. However, the rejection under 35 U.S.C. 103(a) over the prior art of record and the partial rejection under 35 U.S.C. 112, second paragraph are maintained.

2. It is noted that Applicant has amended the rejected claims under 35 U.S.C. 112, second paragraph partially as suggested by the Examiner, rendering the rejection pertaining thereto moot. Thus, the rejection for the claims which have been amended according the Examiner's suggestion have been withdrawn, but, issues in the claims which have not been amended and have been argued by Applicant are maintained for the same reasons discussed in the previous Office action as reiterated below:

CLAIMS REJECTION-35 U.S.C. 112 2nd PARAGRAPH

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-23 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 16 and 23 are indefinite and confusing in the recitation "a common laboratory agent" because the phrase "common laboratory agent" is not defined in the specification or in the claims. The phrase would encompass any laboratory agent, and as such, the metes and bounds of the claims are not determined.

CLAIMS REJECTION-35 U.S.C. § 103(a)

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-23 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Bensadoun et al., (Analytical Biochemistry, Volume 70, pp. 241-250, 1976) taken with Carraro et al., (Biochem. & Biophys. Res. Commun., Vol. 200, No. 2, pp. 916-924, 1994).

Bensadoun et al., disclose like the instantly claimed invention a method of protein precipitation in dilute solution by mixing the protein solution with an acidic agent and/or component such as Trichloracetic acid (TCA) and then adding or introducing into the

mixture of the protein precipitate-forming agent such as sodium deoxycholate and a salt such as sodium chloride (See abstract and materials and methods). Hence, the reference clearly discloses a protein-precipitating agent intended for protein assay comprising an acidic component, a precipitate-forming component and a salt, and a method of protein precipitation thereof. On Table 1, the reference shows some of the most commonly used reagents such as organic solvents (e.g., ethylene glycol, glycerol, acetylacetone, etc.) and polysaccharides (e.g., sucrose, fructose, mannose, xylose, glucose, etc.) in the analysis and in the purification of biological substances, particularly in the process of Lowry protein determination. Thus, the prior art clearly discloses a protein-precipitating agent comprising an acidic component, a precipitate-forming component and reagents such as organic solvents and polysaccharides and a method of preparation of protein sample solution for analysis thereof intended for the purpose of a protein assay.

The primary reference of Bensadoun et al. differs from claims 1-23 in not teaching the use of specific detergent such as SDS and organic solvents such as acetone and alcohol. However, Carraro et al., teach of a two-step precipitation method that removes free SDS detergent from diluted solutions of proteins, thus, allowing for the recovery and quantification of the proteins themselves. In the method, proteins, which have been solubilized with SDS, are first treated with a solution of potassium phosphate, which serves to precipitate free SDS detergent. The protein-containing supernatant is then treated with a trichloracetic acid solution and potassium chloride, which serves to precipitate the proteins. The protein content is then determined by the

Lowry method, which comprises the steps of adding the protein precipitate to an alkaline copper solution and adding a Folin reagent (See e.g., pages 916-918). Therefore, Carraro et al. teach of a method for precipitating proteins in a solution containing a detergent (i.e., SDS), which comprises the steps of treating a protein solution containing SDS with an acidic component and a salt. Although, the secondary reference of Carraro et al. fail to teach that proteins can be precipitated by the combination of the acidic component with a precipitate-forming component such as deoxycholate. However, the primary reference of Bensadoun et al., teach of a protein assay in which protein is precipitated by treating the protein solution with a combination of an acidic component such as trichloracetic acid and sodium deoxycholate. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention was made to precipitate the proteins in the method of Carraro et al. with a combination of an acidic agent and deoxycholate rather than an acidic agent and potassium chloride, since Bensadoun et al., teach that such a combination is another, known effective means to precipitate protein equivalent in function to the combination taught by Carraro et al.

With respect to the use of specific organic solvents such as acetone and alcohol; although, none of the prior art cited disclose the use of organic solvents such as acetone and alcohol; however, as admittedly acknowledged on page 3, last paragraph in the instant specification clearly states "Organic solvents such as acetone and alcohol have been used for precipitation of protein in aqueous solution." Thus, in view of this, it is clear that one of ordinary skill I the art would be able to employ organic solvents such

as acetone and alcohol for precipitation of protein. Therefore, in view of the above and in view of the teachings of the prior art, one of ordinary skill in the art would have been motivated to use a composition of a protein-precipitating agent, a method of protein precipitation thereof for a protein assay. Thus, the instant invention's method of preparation of protein sample solution for analysis, protein-precipitating agent comprising an acidic component, a precipitate-forming component and a salt, and a method of protein precipitation thereof for protein assay; which fall within the scope of the prior art protein-precipitating agent and method of protein precipitation thereof would have been prima facie obvious from said prior art disclosure to a person of ordinary skill in the art at the time the invention was made in the absence of sufficient objective factual evidence or unexpected results to the contrary.

ARGUMENTS ARE NOT PERSUASIVE

CLAIMS REJECTION-35 U.S.C. 112, 2nd PARAGRAPH

5. Claims 1-23 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments filed 1/12/04 have been fully considered but they are not persuasive. Applicant has argued that one of ordinary skill in the art will understand that the terminology "a common laboratory agent" refers to those chemical agents when present in protein solution do not either render the protein in the solution insoluble or destroy the protein. However, claims 1, 16 and 23 are not rejected as being indefinite

and confusing on the basis of chemical agents when present in protein solution to render the protein in the solution insoluble or destroy the protein as argued by Applicant. Rather, as stated above, claims 1, 16 and 23 are indefinite and confusing in not defining the phrase "common laboratory agent" in the specification or in the claims. The phrase would encompass any laboratory agent, and as such, the metes and bounds of the claims are not determined. Thus, in view of the above, the definiteness of the claims are important to allow others who wish to enter the market place to ascertain the boundaries of protection that are provided by the claims. See *Ex parte Kristensen*, 10 USPQ 2d. 1701, 1703 (PTO Bd. App. & Inter. 1989). Hence, in order to obviate the above rejection, it is suggested gain that Applicant amends the claims to particularly point out and distinctly claim the subject matter, which Applicant regards as the invention.

CLAIMS REJECTION-35 U.S.C. § 103(a)

6. The rejection of claims 1-23 under 35 U.S.C. 103(a) as being unpatentable over Bensadoun et al. (Analytical Biochemistry, Volume 70, pp. 241-250, 1976) taken with Carraro et al. (Biochem. & Biophys. Res. Commun., Vol. 200, No. 2, pp. 916-924, 1994).

Applicant's arguments that the primary reference of Bensadoun et al. teaches **first** mixing protein solution with sodium deoxycholate and **then** adding or mixing trichloric acid not, as asserted in the Office Action, **first** acid and then sodium deoxycholate. Thus, applicant submits that one of skill in the art would certainly expect

that the order of mixing of various agents would affect the outcome of the method is unpersuasive. Contrary to Applicant's arguments in regard to the order of mixing the protein solution with an acid to formulate a protein precipitant, the reference of Bensadoun et al. clearly teaches the precipitation of a protein in dilute solution by mixing the protein solution with an acidic agent and/or component such as trichloracetic acid and then adding or introducing into the mixture of the protein precipitate-forming agent such as sodium deoxycholate and a salt such as sodium chloride (See e.g., page 243, last paragraph). Thus, regardless the order, the reference clearly discloses a protein-precipitating agent intended for protein assay comprising an acidic component, a precipitate-forming component and a salt, and a method of protein precipitation thereof as recited in claims 1, 16 and 23.

In regard to Applicant's allegation that in the presence of SDS in protein solution, Bensadoun et al. would not work is unpersuasive because the Examiner has demonstrated that the secondary reference of Carraro et al., teach of a two-step precipitation method that removes free SDS detergent from diluted solutions of proteins, thus, allowing for the recovery and quantification of the proteins themselves. In the method, proteins, which have been solubilized with SDS, are first treated with a solution of potassium phosphate, which serves to precipitate free SDS detergent. The protein-containing supernatant is then treated with a trichloracetic acid solution and potassium chloride, which serves to precipitate the proteins. The protein content is then determined by the Lowry method, which comprises the steps of adding the protein precipitate to an alkaline copper solution and adding a Folin reagent (See e.g., pages

916-918). Therefore, Carraro et al. teach of a method for precipitating proteins in a solution containing a detergent (i.e., SDS), which comprises the steps of treating a protein solution containing SDS with an acidic component and a salt. Although, the secondary reference of Carraro et al. fails to teach that proteins can be precipitated by the combination of the acidic component with a precipitate-forming component such as deoxycholate. However, the primary reference of Bensadoun et al. teaches of a protein assay in which protein is precipitated by treating the protein solution with a combination of an acidic component such as trichloracetic acid and sodium deoxycholate. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention was made to precipitate the proteins in the method of Carraro et al. with a combination of an acidic agent and deoxycholate rather than an acidic agent and potassium chloride, since Bensadoun et al. teach that such a combination is another, known effective means to precipitate protein equivalent in function to the combination taught by Carraro et al. It is noted that Applicant has alleged that the combination of SDS in Bensadoun's protein solution would not work, however, for Applicant to validate such allegation, Applicant has to provide a side by side comparison showing that using SDS in Bensadoun et al. method of protein precipitation in dilute solution by mixing the protein solution with an acidic agent would not work. Nevertheless, Applicant is cautioned that this is not a invitation to prolong the prosecution of After Final rejection.

With respect to Applicant's assertion that Bensadoun et al. describe the use of sodium chloride for the correction of the reaction blank and not for the "method of protein precipitation in dilute protein solution" as claimed by the Examiner is noted.

Contrary to Applicant's assertion and as admittedly acknowledged by Applicant by stating that it is noted that Bensadoun et al. page 248, last paragraph recites "[t]his blank contribution was eliminated by adjusting the morality of the sample to 1M NaCl before protein precipitation". Thus, this is a clear indication that the NaCl salt was used in the process of protein precipitation in dilute protein solution.

In regard to Applicant's arguments that as far as the listed agents in Table 1 are concerned, none of the agents were used by Bensadoun et al. for protein precipitation as asserted in the Office Action is unpersuasive because Table 1 was used to demonstrate some of the most commonly used reagents such as organic solvents (e.g., ethylene glycol, glycerol, acetylacetone, etc.) and polysaccharides (e.g., sucrose, fructose, mannose, xylose, glucose, etc.) in the analysis and in the purification of biological substances, particularly in the process of Lowry protein determination. Thus, the prior art clearly discloses a protein-precipitating agent comprising an acidic component, a precipitate-forming component and reagents such as organic solvents and polysaccharides and a method of preparation of protein sample solution for analysis thereof intended for the purpose of a protein assay.

Further, Applicant has argued that the applied references, alone or in combination, do not teach or suggest the presently claimed method. In particular, the cited prior art fails to reach the scope of the presently claimed invention, more specifically, quantitative recovery, SDS-free proteins, and applicability to all proteins without requiring any specific control of temperature, solutes, and pH of solutions is noted. Contrary to Applicant's arguments, the claims recite **substantially free** from

non-protein agent and **not** free from non-protein agent as argued by Applicant. The limitation Applicant argued with (i.e., SDS-free proteins, and applicability to all proteins without requiring any specific control of temperature, solutes, and pH of solutions) is not recited in the rejected claims(s). Nevertheless, the claims are interpreted in light of the specification, limitation from specification are not read into claims. See *In re Geuns*, 988 F.2nd 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, Applicant's argument is not commensurate to the scope of the claims.

Therefore, in view of the above and in view of the teachings of the prior art, one of ordinary skill in the art would have been motivated to use a composition of a protein-precipitating agent, a method of protein precipitation thereof for a protein assay. Thus, the instant invention's method of preparation of protein sample solution for analysis, protein-precipitating agent comprising an acidic component, a precipitate-forming component and a salt, and a method of protein precipitation thereof for protein assay. Thus, it is made obvious by the combined teachings of the prior art since the instantly claimed invention which falls within the scope of the combined teachings of the prior art method would have been *prima facie* obvious from said prior art disclosure to a person of ordinary skill in the art because as held in host of cases including *Ex parte Harris*, 748 O.G. 586; *In re Rosselete*, 146 USPQ 183; *In re Burgess*, 149 USPQ 355 and as exemplified by *In re Best*, "the test of obviousness is not express suggestion of the claimed invention in any and all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them".

ACTION IS FINAL

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION AND FUTURE CORRESPONDANCE

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Mohamed/AAM

April 26, 2004

ROBERT A. WAX
PRIMARY EXAMINER